

Supplement Table S1**Signal molecules and exogenous nutrients that regulate the browning of white fat**

Classification	Name	Function	Mechanism of action	Origin	Year	References
Nutrients	Sesamol	Inhibit the increase in the number and quality of lipid droplets in brown adipose tissue, and promote the expression of brown fat marker genes	Inhibit the mRNA levels of white adipogenic genes PPAR α , ACACA, SREBP-1c and FASN; promote the expression of brown fat marker genes such as UCP1, FGF21, COXII	Endogenous	2020	[62]
Nutrients	Resveratrol	Promote browning of white adipose tissue	Resveratrol activates SIRT1 to enhance the level of PPAR γ deacetylation, reduces adipogenesis and lipid accumulation, and promotes the rate of lipolysis. SIRT1-mediated PPAR γ deacetylation can promote the browning of white fat	Endogenous	2014	[75]
Nutrients	Ellagic acid	Inhibit the transformation of pre-adipocytes into mature adipocytes and promote the browning of white fat	Down-regulate the expression of PPAR γ , C/EBP β and C/EBP α in lipid synthesis-related proteins, and up-regulate the expression of BAT marker proteins UCP-1 and PGC-1 α in WAT	Endogenous	2019	[78]

Nutrients	Flavan 3 alcohol	The proliferation and differentiation of brown adipocytes and the related regulation process of white adipocyte browning that may be involved	After treatment with flavan-3 alcohol, the sympathetic nerve activity of mice increased, the content of no adrenaline increased, and the mRNA expression of UCP1 increased	Endogenous	2018	[82]
Nutrients	Epicatechin	Up-regulate the expression of brown adipose tissue to induce fat browning	Increase the expression level of PGC1 α , TFAM, SIRT1, SIRT3, UCP1, etc.	Endogenous	2017	[84]
Nutrients	Capsaicin	Promote browning of white adipose tissue	The TRPV1 channel-dependent intracellular Ca ²⁺ increase and the phosphorylation of Ca ²⁺ /calmodulin-activated protein kinase II and AMP-activated kinase promote Sirtuin-1 expression and activity, thereby triggering white adipocyte browning	Endogenous	2016	[86]
Nutrients	Curcumin	Induces browning of white adipocytes	Promote the expression of β 3AR gene in inguinal white adipocytes, thereby increasing plasma norepinephrine levels; Secretion of interleukin (IL)-4 and/or IL-13 pathway to induce polarization of M2 macrophages and thus induce white adipocyte browning"	Endogenous	2015;2016	[90];[91]

Nutrients	Berberine	Increase thermogenesis of brown fat cells and promote the browning of white fat cells	Berberine increases the expression of UCP1 and other thermogenic genes in white and BAT and primary adipocytes through mechanisms involving AMPK and PGC-1 α	Endogenous	2019	[94]
Nutrients	Quercetin	Acts on fat cells and increases mitochondrial biogenesis to induce browning	Quercetin increased the expression of UCP1 and Elovl). The specific mechanism is reflected in the quercetin AMP-activated protein kinase (AMPK)/sirtuin1/PGC1 α pathway	Endogenous	2021	[102]
Nutrients	Fucoxanthin	Improve insulin resistance and lower blood sugar levels, with potential anti-obesity effects	The intake of fucoxanthin increases the mRNA expression of β 3 adrenergic receptor in WAT, which may be the reason for adaptive thermogenesis by stimulating the excitement of the sympathetic nervous system and up-regulating the expression of UCP1	Endogenous	2005	[107]
Nutrients	Menthol	Enhance browning of WAT and improve diet-induced obesity	Menthol-induced TRPM8 activation, up-regulating the expression levels of UCP-1 and PGC-1 α	Endogenous	2017	[110]
Nutrients	Chlorogenic acid	Induces browning of white adipocytes	Chlorogenic acid exerts anti-diabetic and anti-obesity effects through AMPK pathway, enhancing the expression of PPAR γ , PRDM16 and PPGC-1 α in brown and white adipose tissue	Endogenous	2020	[113]

Nutrients	Chrysin	Reduce lipogenesis and lipogenesis, increase fat oxidation and induce browning	By AMPK activation, chrysin significantly up-regulates the expression of PGC-1 α , UCP1, PRDM16, PPAR family and other browning genes in 3T3 preadipocytes; Stimulates the expression of PLIN, increases the anti-obesity effect of chrysin and promotes the recruitment of brown fat in white adipocytes	Endogenous	2016	[116]
Nutrients	Cinnamaldehyde	Inhibit the hypertrophy of adipose tissue and induce the browning of white adipose tissue	By enhancing the expression of UCP1 in brown adipose tissue and the expression of PPAR γ , PRDM16 and PGC-1 α proteins in brown and white adipose tissue	Endogenous	2017	[120]
Nutrients	Luteolin	Promote differentiation of primary brown cells and subcutaneous fat cells to brown	After luteolin treatment, the protein levels of UCP1, PGC1 α and SIRT1 and the phosphorylation levels of AMPK α and ACC increased	Endogenous	2016	[122]
Nutrients	Taurine	Induces browning of white adipose tissue	Dependent on AMPK signal-mediated induction of PGC1mRNA in white adipocytes	Endogenous	2019	[124]
Nutrients	Emodin	Promote browning in scWAT and activate BAT activity	Increased beige adipocyte markers, such as mRNA in Cd137, Tmem26 and Tbx1scWAT, and UCP1, CD36, FATP4, PPAR α , and inhibitory protein expression in scWAT and BAT	Endogenous	2021	[126]

Nutrients	3'-hydroxydaidzein	Induces browning of white adipose tissue	Increase PRDM16, C/EBP β , p-p38, SIRT1, PGC1 α and UCP1 protein expression	Endogenous	2020	[127]
Nutrients	Rice bran	Promote browning of white adipose tissue	Significantly up-regulate the expression of UCP1 protein and coding genes, and down-regulate the expression of TCF21 and HOXC8 (WAT-specific proteins). In addition, RRB, irb and irbs also effectively increased the levels of PRDM16 and PGC-1 α	Endogenous	2020	[129]
Nutrients	Grape pomace extract	Promote the formation of brown-like fat cells	GPE prevents palmitate-mediated down-regulation of FNDC5/irisin protein expression and secretion through PGC-1 α activation, and up-regulates the expression of UCP-1 in white adipose tissue (WAT)	Endogenous	2020	[131]
Nutrients	Purple Sweet Potato	Promote browning of white adipose tissue	Significantly up-regulate the expression of PGC1 α and UCP-1	Endogenous	2021	[132]
Nutrients	Dietary Apple Polyphenols	Promote browning of white adipose tissue	—	Endogenous	2020	[133]
Nutrients	Strawberry methanol extract	Promote browning of white adipose tissue	—	Endogenous	2020	[134]
Nutrients	Dietary silk peptide	Promote browning of white adipose tissue	—	Endogenous	2020	[135]
Nutrients	Lactobacillus amylophilus KU4	Promote browning of white adipose tissue	—	Endogenous	2019	[136]

Nutrients	Chitosan and Chitooligosaccharides	Promote browning of white adipose tissue	—	Endogenous	2019	[137]
Nutrients	Sargassum	Promote browning of white adipose tissue	—	Endogenous	2020	[138]
Nutrients	Freeze-dried Maqui (Aristotelia chilensis) berries	Promote browning of white adipose tissue	—	Endogenous	2019	[139]
Nutrients	Cardamom	Promote browning of white adipose tissue	—	Endogenous	2019	[140]
Nutrients	Standardized extract of psoralen seeds prenylated flavonoids	Promote browning of white adipose tissue	—	Endogenous	2019	[141]
Nutrients	Fermented Cordyceps Militaris Extract	Promote browning of white adipose tissue	—	Endogenous	2019	[142]
Nutrients	Genistein	Promote browning of white adipose tissue	—	Endogenous	2019	[143]
Nutrients	Broccoli	Promote browning of white adipose tissue	—	Endogenous	2018	[144]
Nutrients	Allicin	Promote browning of white adipose tissue	—	Endogenous	2019	[145]

Signal molecule	Glucocorticoid	Inhibit the browning of white fat	GC can significantly down-regulate the level of UCP-1, but when the inhibitor RU486 is given, the expression level of brown functional genes such as UCP-1 increases significantly; GC regulates the expression of miR-27b through the GRE binding region of the upstream promoter region of miR-27b and inhibits the expression of its target gene PRDM16	Exogenous	2015	[146]
Signal molecule	NRG4	Has great potential in promoting the browning of white fat	The NRG4 synthesized in BAT is activated and phosphorylated under the combined action of protease and extracellular active protein fragments, and the expression of SREBP-1c is also significantly reduced. Changes in these factors reduce the transcription of ACC, SCD1 and FASN	Endogenous	2018	[150]
Signal molecule	Leptin	Participate in activating brown fat thermogenesis	Promote the expression of UCP1 and increase the mRNA level of UCP2 by 63% Sh2b1 neurons that mediate the sympathetic nervous system	Endogenous	2001;2020	[153];[154]
Signal molecule	Catecholamine	Promote browning of white adipose tissue	Catecholamines bind to G protein-coupled β -adrenergic receptors and activate adenylate cyclase (AC), which leads to an increase in cAMP to activate protein kinase A (PKA) and phosphorylate hormone-	Endogenous	2017	[156]

			sensitive lipase (HSL). Causes the browning of white fat			
Signal molecule	FGF21	Promote the browning of white adipose tissue; promote the recruitment of beige fat cells	FGF21 up-regulates the level of PGC-1 α ; at the same time, FGF21 acts in an autocrine/paracrine manner, thereby increasing the expression of UCP1 and other thermogenic genes in adipose tissue	Endogenous	2017;2012	[157];[48]
Signal molecule	BMP-9	Convert white adipose tissue into brown adipose tissue; Promote the recruitment of beige fat cells	BMP-9 can transform white adipose tissue into brown adipose tissue by inhibiting liver gluconeogenesis; BMP-9 enhances the expression of fibroblast growth factor 21 and inhibits obesity, while FGF21 promotes the recruitment of beige adipocytes by up-regulating the protein expression of PGC1- α	Endogenous	2020;2016	[160];[161]
Signal molecule	Telmisartan	Induces browning of white adipocytes	Telmisartan induces M2 marker expression in a concentration-dependent manner in mouse macrophages, and PPAR γ plays a key role in M2 polarization and white adipocyte browning; Telmisartan increases catecholamine (CA) and intracellular tyrosine hydroxylase (TH) mRNA levels	Endogenous	2019	[162]

Signal molecule	IRISIN	Induces browning of white adipose tissue	Irisin circulating in the adipose tissue can induce the browning of white fat by activating the ERK and p38MAPK signaling pathways, thereby increasing the expression of UCP1	Endogenous	2014	[60]
Signal molecule	Prostaglandin	Promote brown fat formation and white adipose tissue browning	Induced by cold exposure, it plays a key role in the formation of brown fat cells and white adipose tissue browning through the COX-2/PG pathway By activating GC-A, it promotes the production of cGMP and then participates in the metabolic process. Through protein kinase G and ion channels, cGMP mediates the biological effects of ANP; Up-regulated the expression of UCP1 and other fat cell browning-related genes, increasing mitochondrial oxidative metabolism and fat oxidation	Endogenous	2018	[165].
Signal molecule	Atrial natriuretic peptide	Induces browning of white adipose tissue	By activating GC-A, it promotes the production of cGMP and then participates in the metabolic process. Through protein kinase G and ion channels, cGMP mediates the biological effects of ANP; Up-regulated the expression of UCP1 and other fat cell browning-related genes, increasing mitochondrial oxidative metabolism and fat oxidation	Endogenous	2008;2014	[168];[169]
Signal molecule	mTORC1	Induces browning of white adipose tissue	β -adrenaline can stimulate the mTORC1/S6K1 pathway and activate the induced fat browning	Endogenous	2016	[171]
Signal molecule	PGC-1 α	Promote the browning of white adipose tissue; activate thermogenesis of brown adipose tissue	Increase the expression of UCP1 and CIDEA; promote the division of mitochondria; increase the uncoupling activity of mitochondria	Endogenous	2017;2011	[41];[56]

Signal molecule	Adrenaline	Activate brown fat	Increase the expression of genes related to thermogenesis and lipid metabolism; promote the accumulation of beige fat in subcutaneous fat	Endogenous	2019	[43]
Signal molecule	HDAC1	The negative regulator of brown fat thermogenesis	Cold stimulation and B-adrenergic receptor activation can separate HDAC1 from the promoter region of brown fat-specific genes, thereby promoting the expression of brown fat-specific genes	Endogenous	2016	[51]
Signal molecule	JAK2		JAK2 and UCP1 are both elevated in brown fat exposed to cold	Endogenous	2013	[52]
Signal molecule	ATF2	Participate in the regulation of cold exposure on the adaptive thermogenesis of adipose tissue	—	Endogenous	2020	[53]
Signal molecule	Zfp516	Participate in the regulation of cold exposure on the adaptive thermogenesis of adipose tissue	—	Endogenous	2015	[54]
